IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Xu et al.

Application No.: 10/054,387

Filing Date: January 22, 2002

Title: MHC CLASS II ANTIGEN PRESENTING CELLS CONTAINING OLIGONUCLEOTIDES WHICH INHIBIT Ii PROTEIN EXPRESSION

Art Unit: 1634

Examiner: Fredman, J.

Docket No.: REH-2011

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with The United States Postal Service as First Class Mail in an envelope Addressed to Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on 12/17/04

PIERCE ATWOOD

Tammy Morton 12/17/04

DECLARATION UNDER 37 CFR 1.132

Commissioner of Patents

P.O. Box 1450

Alexandria, VA 22313-1450

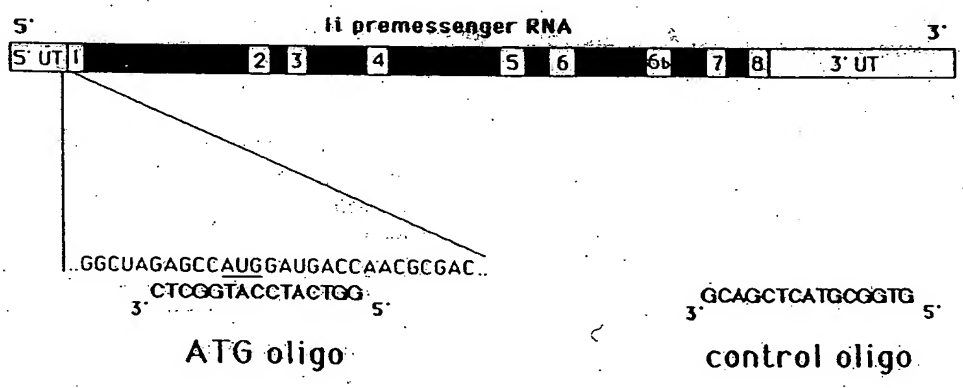
Dear Sirs:

1. My name is Kevin Farrell and I am a registered Patent Attorney (Registration No. 35,505).

2. On June 11, 1996 I filed with the US Patent Office US Application No. 08/661,627 (now US Patent No. 5,726,020) which included claims directed toward antisense methods and compositions useful for displaying an autodeterminant peptide, in association with an MHC class II protein, on the surface of an MHC class II-positive

antigen presenting cell. During the course of prosecution, the Patent Office cited Bertolino et al. (*Int. Immunol.* 3: 435-443 (1991)). Method and composition claims directed toward the antisense technology were placed in condition for allowance by narrowing the scope of the claims to recite specifically exemplified oligonucleotides.

A Continuation-in-Part application claiming priority to US Application No. 08/661,627 (through an intervening Continuation, US Application No. 09/036,746, now abandoned) was filed on December 4, 1998. This Continuation-in-Part application contained substantially more data relating to antisense methods and compositions useful for displaying an autodeterminant peptide, in association with an MHC class II protein, on the surface of an MHC class II-positive antigen presenting cell, relative to the priority application which issued as US Patent No. 5,726,020 (the '020 patent). The claim strategy employed at the time of filing was to seek more generic claim coverage than the claims which issued in the '020 patent by specifically excluding the oligonucleotide 3'-CTCGGTACCTACTGG-5' disclosed in Fig. 2 of Bertolino et al. (*Int. Immunol.* 3: 435-443 (1991)), which is reproduced below.



As of December 4, 1998, I was aware of the fact that the oligonucleotide 3'-CTCGGTACCTACTGG-5' as disclosed by Bertolino et al. had been designed to interact with the AUG site of the mRNA for murine Ii protein. It was noted, however, on page 5 of the application filed on December 4, 1998:

> An antisense oligonucleotide interacting with the AUG site of the mRNA for Ii protein has been described to decrease MHC class II presentation of exogenous antigen (Bertolino et al., *Internat. Immunology* 3: 435-443 (1991)). However, the effect on the expression of Ii protein and on the presentation of endogenous antigen by MHC class II molecules were not examined.

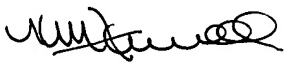
In order to effect the exclusion of the referenced oligonucleotide, the order of oligonucleotides was copied directly from Fig. 2 of the Bertolino et al. reference (in the 3' – 5' orientation, as disclosed by Bertolino) in 3 locations in the priority application as filed: on page 7, in Claim 1 and in Claim 50. Additional evidence of Applicant's intent is attached as Exhibit A. Exhibit A is a cover sheet and first page of a facsimile to inventor Dr. Robert Humphreys dated approximately three weeks prior to the filing date of the priority application. Draft Claim 1 clearly evidences Applicant's intention to exclude the sequence disclosed by Bertalino et al.

Almost two years after US Application No. 08/661,627 was filed, I filed a Response to a Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures (paper filed November 6, 2000). The filing included a request to amend the Specification by incorporating an attached Sequence Listing. SEQ ID NO: 1 is shown as ctcggtacctactgg which corresponds to the order of nucleotides as shown elsewhere in the Specification. However, the rules governing the preparation and filing of a Sequence Listing indicate that the order of nucleotides should be presented in the 5' – 3' direction. Thus by the submission of the Sequence Listing, I inadvertently added new matter to the application in contradiction to the following statement which was included with the filing:

> Applicants' Attorney hereby states that the above amendments to the Specification and Claims include no new matter.

This assignment of orientation, which occurred inadvertently and by default, was inconsistent with that intended at the time of filing and was an error comprising new matter.

3. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signature	
Name	Kevin M. Farrell.
Date	12/17/04

P0068017.DOC

EXHIBIT A

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November 12, 1998

FACSIMILE COVER SHEET

FAXED 11/12/98

TO: Robert E. Humphreys, M.D., Ph.D.

FAX NUMBER: (508) 831-3521

FROM: Shayne Huff SH

SUBJECT: *Selective Inhibition of Ii Expression*
Our Reference No.: REH-2005

THERE WILL BE 13 PAGES INCLUDING THIS COVER SHEET.
CONFIRMATION WILL FOLLOW: YES ___ NO X

Bob:

Upon going through the detailed description in depth, a few relatively minor modifications have been made to the claims. Following is the latest draft. Regarding our discussion about the term "MHC class II-positive antigen presenting cell" and alternatives, the claims use the initial term, which I have defined within the specification as a cell which functions as an antigen presenting cell, either naturally, or due to *in vitro* manipulation. This is an attempt to balance accuracy with brevity. A few of the claims contain bracketed additions, which will more specifically identify the subject matter, if they meet with your approval regarding content.

CLAIMS

DRAFT

1. A specific regulator of Ii protein expression or immunoregulatory function, the oligonucleotide [BERTOLINO OLIGO] being specifically excluded.

2. The specific regulator of Claim 1 which functions through the formation of a duplex molecule with an RNA molecule encoding mammalian Ii protein, the formation of the duplex molecule functioning to inhibit Ii protein synthesis at the translation level.

3. The specific regulator of Claim 2 comprising a copolymer comprised of nucleotides, being characterized by the ability to hybridize specifically to the RNA molecule encoding mammalian Ii protein.

4. The specific regulator of Claim 2 comprising an expressible reverse gene construct, comprising a DNA molecule which encodes a first RNA molecule which is complementary to a segment of a second RNA molecule which encodes a mammalian Ii protein, the first RNA molecule having the ability to hybridize with the second RNA molecule thereby inhibiting translation of the second RNA molecule.

5. The specific regulator of Claim 1 comprising a copolymer comprised of nucleotides, being characterized by the ability to hybridize specifically to a gene encoding mammalian Ii protein.

6. The specific regulator of Claim 1 comprising an organic molecule of 20 to 1000 Daltons.

7. The specific regulator of Claim 3 wherein the nucleotides are joined to a backbone which includes moieties selected from the group consisting of phosphodiester,